PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control

	Substitute for form 1449B/PTO				Complete if Known	
	INFORMATI	ON DISCLO	SURE	Application Number	10/049,373	
STATEMENT BY APPLICANT				Filing Date	06/21/2002	
				First Named Inventor	Isao ISHIDA et al.	
Date Submitted: 08/21/2002 (use as many sheets as necessary)			2002	Group Art Unit	Unassigned	
			cessary)	Examiner Name	Unassigned	
Sheet	1	of	3	Attorney Docket Number	051023-0115	

U.S. PATENT DOCUMENTS							
		U.S. Patent	Document		Date of Publication of	Pages, Columns, Lines, Where Relevant	
Examiner Initials"	Cite No.1	Number	Kind Code ² (if known)	Name of Patentee or Applicant of Cited Document	Cited Document MM-DD-YYYY	Passages or Relevant Figures Appear	
		•					
			 				
			 -				
	-		1				

FOREIGN PATENT DOCUMENTS									
Examiner Initials*	Cite No.1	Fa Office ³	reign Petent C Number ⁴	Nocument Kind Cod		Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Cotumns, Lines, Where Relevant Passages or Relevant Figures Appear	Te
TUT	A1	WO	98/37757		A1	Tomizuka et al.	3/09/1998		abs
		ļ							<u> </u>
		 						· · · · · · · · · · · · · · · · · · ·	
			*						
			 						ļ
	-	-							
	i Ti								100

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS							
Examiner initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [®]				
TUT	A2	TOMIZUKA et al., EP0773288 A3, July 9, 1997, Abstract.					
TUT	A3	RAMSDEN, R. et al., "Phenobarbital Induction and Tissue-specific Expression of the Rat CYP2B2 Gene in Transgenic Mice", J. Biol. Chem., 268 (222): 21722-2176 (1993).					
TNT	A4	KAMATAKI, T. et al., "Application of Molecular Technology to Drug Metabolism Studies: Perspectives", Yakubutsu Doutai, 13(3): 280-286 (1997)	yes				
TWT	A5	NELSON et el., "P450 superfamily: update on new sequences, gene mapping, accession numbers and nomenclature," Pharmacogenetics, 6: 1-42, (1986).					

Examiner Signature	there	Date Considered	2/18/05

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See stached Kinds of U.S. Patent Documents. ²Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). *For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. *Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. *Applicant is to place a check merk here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of Information unless it contains a valid OMB control

	Substitute for form 1	14498/	PTO		Complete if Known	
	INFORMATION DIS	SCLO:	SURE	Application Number	10/049,373	
STATEMENT BY APPLICANT				Filing Date	08/21/2002	
	Date Submitted: 0	16/24/2	0002	First Named Inventor	Isao ISHIDA.et al.	
	Date Subilitated. O	1012 112	:002	Group Art Unit	Unassigned	
	(use as many sheets	as nec	essary)	Examiner Name	Unassigned	
Sheet	2	of	3	Attorney Docket Number	051023-0115	

_		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner nitials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	۴
TUT	A6	TOMIZUKA, K. et et., "Functional Expression and Germline Transmission of a Human Chromosome Fragment in Chimaeric Mice". Nature Genetics, 16: 133-143 (1997).	
	A7	JAKOBOVITS, A. et al., "Germ-line Transmission and Expression of a Human-Derived Yeast Artificial Chromosome", Nature, 382: 255-258 (1993).	
	A8	SHIINA, T. et al., "Nucleotide Sequencing Analysis of the 146-Kilobase Segment Around the IkBL and MICA Genes at the Centromeric End of the HLA Class 1 Region", Genomics, 47: 372-382 (1998).	
	A9	HUBERT, R. et al., "BAC and PAC Contigs Covering 3.5 Mb of the Down Syndrome Congenital Heart Disease Region Between D21S55 and MX1 on Chromosome 21", Genomics, 41: 218-226 (1997).	
	A10	Recombinase-Mediated Site-Specific Recombination in Embryonic Stem Cells*, Proc. Natl. Acad. Sci. USA, 93: 6158-6161 (1996).	
	A11	GU, H. et al., "Deletion of a DNA Polymerase β Gene Segment in T Cells Using Cell Type-Specific Gene Targeting", <u>Science</u> , 265: 103-108 (1994).	
	A12	LI, Y., et al., "Establishment of Transgenic Mice Carrying Human Fetus-Specific CYP3A7", Archives of Biochemistry and Biophysics, 239 (2): 235-240 (1996).	
	A13	KAMATAKI, T. et al., "Expression of CYP3A7, a Human Fetus-Specific Cytochrome P450, in cultured Cells and in the Hepatocytes of p53-Knockout Mice", Toxicology Letters, 82/83: 879-882 (1985).	
	A14	KOVALEVA, I. et al., 'Transgenic Yeast Expressing Human Cytochrome P450s Can Serve as a Tool in Studies of the Mechanisms of their Induction by Various Effectors', <u>Biochemical and Biophysical</u> Research Communications, 221(1): 129-132 (1996).	 -
	A15		
	A16	Using Baculovirus", Archives of Blochemistry and Biophysics, 274(2): 481-490 (1989).	
	A17	the Metabolism of Benzo[a]pyrene and Benzo[a]pyrene trans, 7-8-Dihydrodiol*, Molecular Carcinogenesis, 10: 159-168 (1994).	
	A18	WOLF, C., et al., "Use of Transgenic Animals in Understanding Molecular Mechanisms of Toxicity", J. Phar. Pharmacol., 50: 567-574 (1998).	
/	A19	Experimental Pharmacology and Physiology, 25: 783-787 (1998).	
TAT	A20	PINEAU, T. et al., "Neonatal Lethality Associated with Respiratory Distress in Mice Lacking Cytochrome P450 1A2," Proc Natl. Acad. Sci. USA, 92: 5134-5138 (1985).	

Examiner Signature	thace	Date Considered	2118/05

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number, ²See stached Kinds of U.S. Patent Documents, ºEnter Office that issued the document, by the two-letter code (WIPO Standard ST.3), °For Japanese petent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. °Ind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. *Applicant is to place a check mark here if English tanguage Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the Individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Petente, Washington, D.C. 20231.

PTO/SB/08 (08-00) Approved for use through 10/31/2002. OMB 0651-0031

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

	Substitute fi	or form 1449B	/PTO		Complete if Known		
	INFORMATI	ON DISCLO	SURE	Application Number	10/049,373		
STATEMENT BY APPLICANT Date Submitted: 06/21/2002				Filing Date	06/21/2002		
				First Named Inventor	Isao ISHIDA et al.		
				Group Art Unit	Unassigned		
(use as many sheets as necessary)			cessary)	Examiner Name	Unassigned		
Sheet	3	of	3	Attorney Docket Number	051023-0115		

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1 Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		Το
TOUT	A21	LIANG, H. et al., "Cyp1a2(-/-) Null Mutant Mice Develop Normally but Show Deficient Drug Metabolism", Proc. Natl. Acad. Sci. USA, 93: 1671-1676 (1996).	
	A22	GENTER, M. et al., "Role of CYP2AS and 2G1 in Acetaminophen Metabolism and Toxicity in the Olfactory Mucosa of the Cyp1a2(-/-) Mouse", Biochemical Pharmacology, 55: 1819-1826 (1998).	
	A23	LEE, S. et al., "Role of CYP2E1 in the Hepatoxicity of Acetaminophen", The Journal of Biological Chemistry, 271: 20, 12063-12067 (1996).	
	A24	FUNAE, Y. et al., "Drug Metabolism by Human Cytochrome P 450", Bioscience and Industry, 55: (2): 81-86 (1997).	partia
	A25	KAMATAKI, T. et al., "Reports of Anhyo Center Laboratory", Incorporated Foundation, 7: 27-33 (1997).	partia
	A26	ISHIDA et al., "Introduction to Cell Engineering, Experiment Manipulation", Kodansha Publishing, 39: lines 1-4 (1992).	partia
	A27	AlZAWA, S. "Gene Targeting", Biomanual Series 8, Yodosha : 89-105 (1995).	
121	A28	SHIMUZU, M., "III Chromosome and Gene Mapping 7, Method for Introduction of Human Chromosome by Microcell Fusion", Cell Engineering Handbook, Youdosha: 127-132 (1992).	partia

Examiner Signature	than	Date Considered	2/15/05

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ³See attached Kinds of U.S. Patent Documents. ¹Enter Office that issued the document, by the two-letter code (WIPO Standard 87.3). *For Japaness patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. *Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. *Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.